What is Claimed is:

1. A human RNase H1 polypeptide which comprises one or more mutations compared to wild type human RNase H1, wherein the mutant version retains detectable cleavage activity for the RNA strand of an RNA/DNA duplex.

2. The human RNase H1 polypeptide of claim 1 wherein the mutation is a point mutation.

3. The human RNase H1 polypeptide of claim 2 wherein the point mutation is in the basic substrate binding domain.

4. The human RNase H1 polypeptide of claim 3 wherein the point mutation is a lysine-to alanine substitutions at amino acids 226 or 227.

5. The human RNase H1 polypeptide of claim 4 wherein the point mutation is a lysine-to-alanine substitution at both amino acids 226 and 227.

6. The human RNase H1 polypeptide of claim 1 wherein the mutation is a deletion mutation.

7. The human RNase H1 polypeptide of claim 6 wherein the deletion mutation is the deletion of at least a portion of the dsRNA binding domain (region I).

8. The human RNase H1 polypeptide of claim 6 wherein the deletion mutation is the deletion of at least a portion of region II.

9. The human RNase H1 polypeptide of claim 6 wherein the deletion mutation is the deletion of at least a portion of both regions I and II.

10. A composition comprising the human RNase H1 polypeptide of claim 1 and a pharmaceutically acceptable carrier.

11. A human RNase H1 polypeptide which consists solely of the basic substrate binding domain (region III) and which retains detectable cleavage activity for the RNA strand of an RNA/DNA duplex.

12. The human RNase H1 polypeptide of claim 11 which has an initial cleavage rate for the RNA strand of an

RNA/DNA duplex which is at least 50% of the initial cleavage rate for a wild type human RNase H1.

13. A composition comprising the human RNase H1 polypeptide of claim 11 and a pharmaceutically acceptable carrier.

14. A human RNase H1 polypeptide which comprises one or more mutations compared to wild type human RNase H1, wherein the mutant version retains detectable cleavage activity for the RNA strand of an RNA/DNA duplex and wherein the cleavage pattern obtained is substantially identical to that of a wild type human RNase H1.

15. The composition of claim 14 wherein the cleavage pattern consists of cleavage sites from 8 to 12 nucleotides from the 5'-RNA/3' DNA terminus of the RNA/DNA duplex.

16. A composition comprising the human RNase H1 polypeptide of claim 14 and a pharmaceutically acceptable carrier.

17. A composition comprising a human RNase H1 polypeptide which comprises one or more mutations compared to wild type human RNase H1, wherein the mutant version retains detectable cleavage activity for the RNA strand of an RNA/DNA duplex and wherein the cleavage pattern obtained is broader than that of a wild type human RNase H1.

18. The composition of claim 17 wherein the cleavage pattern consists of cleavage sites from 7 to 13 nucleotides from the 5'-RNA/3' DNA terminus of the RNA/DNA duplex.

19. A composition comprising the human RNase H1 polypeptide of claim 17 and a pharmaceutically acceptable carrier.

20. A human RNase H1 polypeptide which comprises one or more mutations compared to wild type human RNase H1, wherein the mutant version retains no detectable cleavage activity for the RNA strand of an RNA/DNA duplex.

21. The human RNase H1 polypeptide of claim 20 which is a dominant negative mutant.

22. A method of enhancing inhibition of expression of a selected protein by an antisense oligonucleotide targeted to an RNA encoding the selected protein comprising:

(a) providing an antisense oligonucleotide targeted to an RNA encoding a selected protein whose expression is to be inhibited;

(b) allowing said oligonucleotide and said RNA to hybridize to form an oligonucleotide-RNA duplex;

(c) contacting said oligonucleotide-RNA duplex with a human RNase H1 polypeptide of claim 1, 11, 14 or 17, under conditions in which cleavage of the RNA strand of the oligonucleotide-RNA duplex occurs, whereby inhibition of expression of the selected protein is enhanced.

23. The method of claim 22 wherein the human RNase H1 polypeptide is enriched or overexpressed.

24. The method of claim 23 wherein the human RNAse H1 polypeptide is exogenously added.

25. The method of claim 23 wherein the human RNase H1 polypeptide is an isolated, purified human RNase H1 polypeptide.

26. A method of inhibiting expression of a selected protein by an antisense oligonucleotide targeted to an RNA encoding the selected protein comprising:

(a) providing an antisense oligonucleotide targeted to an RNA encoding a selected protein whose expression is to be inhibited;

(b) allowing said oligonucleotide and said RNA to hybridize to form an oligonucleotide-RNA duplex;

(c) contacting said oligonucleotide-RNA duplex with a human RNase H1 polypeptide of claim 1, 11, 14 or 17, under conditions in which cleavage of the RNA strand of the oligonucleotide-RNA duplex occurs, whereby expression of the selected protein is inhibited.

27. The method of claim 26 wherein the human RNase H1 polypeptide is enriched or overexpressed.

28. The method of claim 27 wherein the human RNase H1 polypeptide is exogenously added.

29. The method of claim 27 wherein the human RNase H1 polypeptide is an isolated, purified human RNase H1 polypeptide.

30. A method of eliciting cleavage of a selected cellular RNA target comprising:

(a) providing an antisense oligonucleotide targeted to a selected cellular RNA target to be cleaved;

(b) allowing said oligonucleotide and said RNA to hybridize to form an oligonucleotide-RNA duplex;

(c) contacting said oligonucleotide-RNA duplex with a human RNase H1 polypeptide of claim 1, 11, 14 or 17, under conditions in which cleavage of the RNA strand of the oligonucleotide-RNA duplex occurs, whereby cleavage of the cellular RNA target is elicited.

31. The method of claim 30 wherein the human RNase H1 polypeptide is enriched or overexpressed.

32. The method of claim 31 wherein the human RNase H1 polypeptide is exogenously added.

33. The method of claim 31 wherein the human RNase H1 polypeptide is an isolated, purified human RNase H1 polypeptide.

34. A method of screening oligonucleotides to identify an effective antisense oligonucleotide[s] for inhibition of expression of a selected target protein comprising:

(a) contacting a human RNase H1 polypeptide of claim 1, 11, 14 or 17 with an RNA encoding the selected target protein and an oligonucleotide complementary to at least a portion of the RNA under conditions in which an oligonucleotide-RNA duplex is formed;

(b) detecting cleavage of the RNA of the oligonucleotide-RNA duplex wherein cleavage is indicative of antisense efficacy.

35. The method of claim 34 wherein the human RNase H1 polypeptide is enriched or overexpressed.

36. The method of claim 35 wherein the human RNase H1 polypeptide is exogenously added.

37. The method of claim 35 wherein the human RNase H1 polypeptide is an isolated, purified human RNase H1 polypeptide.

38. An effective antisense oligonucleotide identified in accordance with the method of claim 34.

39. The method of claim 34 further comprising determining the site on the RNA at which cleavage occurs, whereby said site is identified as a RNase H1-sensitive site.

40. The method of claim 34 further comprising identifying an effective antisense oligonucleotide which hybridizes to said RNase H1-sensitive site.

41. The method of claim 34 wherein the oligonucleotide is one of a mixture or library of oligonucleotides.

42. An effective antisense oligonucleotide identified in accordance with the method of claim 40.